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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 07/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,080	ISAKSON ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 2 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *5,8,10 and 12-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,9,11 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection (i.e., see 12/17/03 Response). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/17/03 has been entered. Claims 1-9 were pending. Applicants added claims 10-18 and amended claims 3 and 8. Therefore, claims 1-18 are pending and active in the instant application. However, claims 5, 8, 10 and 12-14 are drawn to non-elected species and/or inventions and thus these claims are/remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim (e.g., see 5/5/04 Response, page 2, last paragraph). Therefore, claims 1-4, 6, 7, 9, 11, 15, 16, 17 and 18 are examined on the merits in this action.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Withdrawn Objections/Rejections

2. The rejections under 35 U.S.C. § 102 are hereby withdrawn in view of Applicants' arguments. The Non-statutory double patenting rejection over claims 1-22 of U.S. Patent No. 6,136,839 is hereby withdrawn in view of Applicants' arguments (the Examiner thanks Applicants for pointing out the typographical error e.g., 12/17/03 Response, pages 42-43). The New Matter rejection under 35 USC 112, first paragraph is hereby withdrawn in view of

Applicants' arguments and/or amendments. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claim Rejections - 35 USC § 112, first paragraph

3. Claims 1-2, 6-7, 9 and 17-18 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

Applicants' claims are drawn to a broad genus of compounds that include an infinite number of "cyclooxygenase-2 (Cox-2) selective inhibitors" (i.e., claims 1-2 and 17-18) and "selective leukotriene B_4 receptor (LTB_4) antagonists" (i.e., claims 1-2, 6-7, 9 and 17-18) wherein no distinguishing structural attributes and/or identifying characteristics are provided other than the purely "functional language" that is used to name the compounds (i.e., their ability to "inhibit" or "antagonize"). The specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form either the Cox-2 inhibitor or the LTB_4 antagonist. Although the specification discloses several examples for both the Cox-2 inhibitors and the LTB_4 antagonists (see Claims 2-9, pages 5-12), the specification and claims do not provide ***any*** guidance as to what structural features ***all*** of these compounds share. In addition, Applicants' specification does not provide a clear definition

as to what constitutes a "selective" Cox-2/LTB_4 inhibitor/antagonist (e.g., see 35 U.S.C. 112, second paragraph rejection, which is incorporated in its entirety herein by reference).

Consequently, it is not possible to "immediately envision" which compounds would be "selective" inhibitors and/or antagonists because there is no common structural attributes and/or other identifying characteristics that can link together ***all*** of the compounds. For example, in *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, the Court stated that, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify ***all*** of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant, listing examples Taisho NS-398, Merck MK-966, etc. that are known in the literature (see

specification, claim 2) is insufficient to teach the entire genus. For example, Applicants' claims are broad enough to encompass antisense-oligonucleotides that selectively "inhibit" the transcription/translation of cycloxygenase-2 over cycloxygenase-1 (e.g., please note that Applicants' definitions for Cox-2/LTB_4 inhibitors/antagonists are vague and indefinite and, as a result, the metes and bounds of the claimed invention cannot be determined i.e., see 35 U.S.C. 112, second paragraph rejections denoted A and B, which are incorporated in their entirety herein by reference). However, Applicants' specification provides no sequence that will achieve such a result and no assay conditions and/or other identifying characteristics that will remedy this defect. Thus, Applicants' specification clearly does not meet the requirements of 35 U.S.C. 112, first paragraph with respect to the ***full scope*** of the claimed invention. Applicants must provide some correlation between the structure and function of the claimed compounds or other identifying characteristics consistent with the PTO's guidelines (e.g., see *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 285 F.3d 1013 (Fed. Cir. 2002) wherein the court adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics ***when coupled with a known or disclosed correlation between function and structure*** ... ." *Enzo*, 296 F.3d at 1324-25 (quoting Guidelines, 66 Fed. Reg. at 1106 (emphasis added)). Consequently, Applicants' claimed scope represents only an invitation to experiment regarding other possible LTB_4 antagonists and Cox-2 inhibitors. In addition, the Examiner notes that it is well settled that claiming only a result (i.e.,

the ability to selectively inhibit Cox-2 and/or LTB_4 inhibitors/antagonists) fails to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result, far beyond those means actually discovered or contemplated by the inventor, so that others would have no incentive thereafter to explore a field already fully dominated. O'Reilly v. Morse, 15 How. 62, In re Fuetterer, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217 ; Siegel v. Watson, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119 .

Response

4. Applicant's arguments directed to the above written description rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive (except for claim 8, see below) for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue that the Written Description Guidelines can be satisfied by a variety of methods (e.g., see examples 1-6 on pages 26-27) including "[b]y sufficient description of a representative number of species by disclosure of relevant structural chemical formulas", which Applicants purport has been met in the instant case presumably referring to the "over 100 examples" of specific compounds that selectively inhibit cycloxygenase-2 and the "over 40 examples" of specific compounds that are selective leukotriene B_4 receptor antagonists that are disclosed in the specification (e.g., see 12/17/03 Response, pages 25-28).

[2] Applicants also argue that the selective Cox-2/LTB_4 inhibitors/antagonists are "known" in the art and, as a result, presumably do not have to be adequately described (e.g., see bottom of page 27).

[3] Applicants argue that their specification provides a "detailed definition" regarding exactly what constitutes a "selective" Cox-2 or LTB_4 inhibitor/antagonist and cites various passages in the specification in support of this position (e.g., see 12/17/03 Response, top of page 28).

[4] Applicants argue that their claims are drawn to two "known" classes of chemical compounds (i.e., Cox-2 selective inhibitors and selective LTB_4 antagonists) and, as a result, the written description only need be so specific as to lead one having ordinary skill in the art to that class of compounds, which has been met in the instant case because "a skilled artisan can readily distinguish members that belong to each class from those that do not" (i.e., a 'selective' compound from a 'non-selective compound') (e.g., see 12/17/03 Response, page 29, last paragraph).

[5] Applicants argue that the inventor in *In re Fuetterer* was allowed to claim their compositions for use in the production of rubber tires using functional language and, as a result, they should be afforded the same opportunity because the "essential qualities" of their invention rest in the "combination" of ingredients (i.e., not in the individual ingredients alone), as was the case in *In re Fuetterer*. In addition, they note that their use of functional language meets the requirements set forth in the Written Description Guidelines because Applicants provide relevant structural chemical formulas for a representative number of species (e.g., see 12/17/03 Response, pages 30-31).

[6] Applicants argue that the present case is distinguishable from *Enzo Biochem* by stating that a single "unknown" compound was at issue in *Enzo* as compared with two "known" compounds in combination here (e.g., see 12/17/03 Response, page 31, middle of the page).

[7] Applicants argue that the present case is distinguishable from *Eli Lilly* by stating that *Eli Lilly* pertained to "unknown and unpredictable [nucleic acid] sequences", which is not the case here because Applicants claims are drawn to a combination of "known" compounds and cite the following excerpt in support of their position at 116 F.2d 1568:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly such a formula is normally an adequate description of the claimed genus

Applicants further note that their claims are drawn to a composition and not the compounds that comprise the composition per se and that they have met all the requirements of the Written Description Guidelines as supported by *Eli Lilly* including and providing relevant structural information and providing a "detailed" description of what constitutes a "selective Cox-2 or LTB_4 inhibitor/antagonist (e.g., see 12/17/03 Response, pages 31-32).

[8] Applicants argue that claims 2, 6, 7 and 9 only have one compound that is described functionally and that claim 8 does not contain any functional language and thus these claims provide even more "identifying" characteristics that would meet the Written Description Guidelines than does claim 1 wherein both compounds are described functionally (e.g., see 12/71/03 Response, pages 32-33).

[9] Applicants argue that University of *Rochester v. G.D. Searle & Co., Inc.* does not apply to the present case because the specification in *Rochester* provided "no knowledge whatsoever of the names of specific compounds which would work", which is not the case here

because Applicants' specification "provides over 100 examples of specific compounds that selectively inhibit cycloxygenase-2 and over 40 examples of specific compounds that are selective leukotriene B_4 receptor antagonists" and, as a result, the Rochester case is inapposite (e.g., see 12/17/03 Response, pages 33-34).

[10] Applicants argue again that there are many ways to adequately describe the claimed invention and submit that there is no requirement for a "correlation between the structure and function." Applicants further reiterate that their claimed invention is adequately described because they provide "relevant structural chemical formulas" and a "detailed" definition for the Cox-2/LTB_4 inhibitors/antagonists (e.g., see 12/17/03 Response, pages 34-35).

This is not found persuasive for the following reasons:

[1] The Examiner acknowledges that there are many ways to satisfy the Written Description Requirement, but contends that this burden has not been met using any of those ways. Specifically, Applicants disclosure fails to provide a "representative" number of species because Applicants' claimed genus (i.e., compositions including Cox-2 selective inhibitors and selective LTB_4 antagonists that are defined solely in terms of their function i.e., their ability to inhibit or antagonize) encompass an infinite number of compounds that fall within an potentially unlimited number of chemical classifications (e.g., see 35 U.S.C. 112, second paragraph "metes and bounds" rejections denoted A and B, which are incorporated in their entirety herein by reference). For example, Applicants' definition of a Cox-2 inhibitor does not preclude compounds that fall within, for example, chemical class 536, subclass 24.5 and, as a result, would not preclude the use of "antisense-oligonucleotide" technology to "selectively inhibit" Cox-2 over Cox-1 (e.g., see specification, paragraph bridging pages 7-8 wherein Applicants

broadly define the term "cyclooxygenase-2 inhibitor" as "embracing" [i.e., comprising] compounds which selectively inhibit cyclooxygenase-2 over cyclooxygenase-1, which would encompass anti-sense oligonucleotides that selectively "inhibit" Cox-2 over Cox-1). However, Applicants specification does not provide any examples of antisense-oligonucleotides or any other relevant information that would allow a person of skill in the art to identify and/or characterize such compounds. Thus, Applicants' specification clearly does not provide a "representative" number of antisense-oligonucleotide chemical formulas. In a similar manner, Applicants' specification also fails to provide examples and/or distinguishing characteristics for potentially an unlimited number of other classes/subclasses of compounds that would fall within the scope of Applicants' broad claims i.e., Applicants' claims are not limited to a particular core structure as was the case in *In re Herschler* (e.g., see again 35 U.S.C. 112, second paragraph "metes and bounds" rejections; see also section **[4]** below with regard to *In re Herschler*).

[2] The general knowledge and level of skill in the art to which Applicants refer do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify ***all*** of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant (e.g., see 35 U.S.C. 112, second paragraph "metes and bounds" rejections denoted A and B, which are incorporated in their entirety herein by reference), listing that fall only within one or two chemical classes of compounds (e.g., see specification, page 3, first full paragraph, wherein only two chemical classes of compounds are listed as LTB_4 antagonists in the prior art i.e., (1) sulfonamides and (2) aryl ethers) is insufficient to teach the entire genus, which encompasses potentially all classes and subclasses of chemical compounds.

In addition, the Examiner notes that it is well settled that claiming only a result (i.e., the ability to selectively inhibit Cox-2 and/or LTB_4 inhibitors/antagonists) fails to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result (i.e., all possible chemical classes and subclasses), far beyond those means actually discovered or contemplated by the inventor (e.g., sulfonamides and/or aryl ethers as LTB_4 antagonists), so that others would have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217 ; Siegel v. Watson, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119.

[3] The Examiner contends that Applicants have not provided **any** definition for a "selective" Cox-2/LTB_4 inhibitor/antagonist let alone a "detailed" definition. The passages cited by Applicants (e.g., see 12/17/03 Response, page 36) notably fail to draw the reader's attention toward the most important parts of the definitions, namely, the subject matter of what is being defined (e.g., see 12/17/03 Response, page 36, wherein the cited passages omit the first sentence of each definition). In both cases, Applicants define (referring to the full definition in the specification) only broad categories of Cox-2/LTB_4 inhibitors/antagonists that "embrace" [i.e., comprise] "selective" inhibitors/antagonists as well as "non-selective" inhibitors/antagonists (e.g., see page 7, lines 28-29, "The term 'cyclooxygenase-2 inhibitor' embraces [i.e., comprise] compounds which selectively inhibit cyclooxygenase-2 ..."; see also page 8, lines 4-5, "The term 'leukotriene B_4 receptor antagonist' embraces [i.e., comprise] compounds which selectively antagonize a leukotriene B_4 receptor ..."). These definitions include both "selective" and "non-selective" inhibitors/antagonists because Applicants use "comprising" terminology that does not

preclude the "non-selective" inhibitors/antagonists from falling within the scope of the definitions (e.g., see Webster's II New Riverside University Dictionary, page 427, wherein the dictionary defines "embrace" as "... **3.** To include, comprise, or contain"). Applicants are not defining what "selective" Cox-2/LTB_4 inhibitors/antagonists are at those recited passages but, rather, what Cox-2/LTB_4 inhibitors are in general (i.e., whether they are "selective" or "non-selective"). In addition, the selectivity ratios and/or IC_{50} values referred to therein only represent "preferred" embodiments and, as a result, are not limiting in any way the scope of the word "selective" (e.g., see page 12/17/03 Response, page 36, "Preferably, the compounds have a cycloxygenase-2 IC_{50} of less than about 0.5 μM ..."). Thus, the "selective" compounds referred to by Applicants represent only "examples" of compounds that could fall within the scope of the broader generic classes of Cox-2/LTB_4 inhibitors/antagonists and, as a result, do not represent a definition for the narrower "selective" Cox-2/LTB_4 inhibitors/antagonists (e.g., see also 35 U.S.C. 112, second paragraph rejections denoted A and B, which are incorporated in their entirety herein by reference).

[4] The Examiner contends that *In re Herschler* does not apply here because Cox-2 selective inhibitors and selective LTB_4 antagonists do not represent a "known" class of compounds and cannot be immediately envisioned like the steroids at issue in *In re Herschler*. The word "steroids" connotes a "core structure" of 4-fused rings that would lead a person of skill in the art to that general class of perhydrocyclopentanophenantrene compounds (e.g., see, Solomons, T. W. G. Organic Chemistry Fifth Edition. New York: John Wiley and Sons. 1992, page 1058, section 23.4A, especially perhydrocyclopentanophenanthrene ring system where 4-fused rings are denoted by A-D in top figure). That is not the case here. Neither the Cox-2

selective inhibitors nor the selective LTB_4 antagonists share a common core structure (e.g., see specification, page 3, first full paragraph, wherein "at least two chemical classes" are denoted for the LTB_4 antagonists i.e., (1) sulfonamides and (2) aryl ethers) that would lead a person of skill in the art to test a particular class of compounds. In addition, Applicants' definition for a Cox-2/LTB_4 inhibitor/antagonist is broad and ambiguous (e.g., see 35 U.S.C. 112, second paragraph rejections denoted A and B, which are incorporated in their entirety herein by reference) and would encompass potentially an unlimited number of chemical classes (i.e., many different core structures). Thus, the present case is distinguishable from *In re Herschler* because nothing in Applicants' specification would lead a person of skill in the art to any particular class of compounds (e.g., a compound with a core structure containing four fused rings) other than trial and error testing (i.e., there is no structure-function relationship and/or other identifying characteristics like having "four fused rings" as in *In re Herschler* to obtain a desired physiological activity). The Examiner also notes that the fact that *In re Herschler* contained "only 1 example" is of no consequence because all of the steroidal compounds contain the same core structure (i.e., there was "only 1 core" structure so only 1 example was sufficient), which is not the case here.

The Examiner also notes that in *Tronzo v. Biomet*, 156 F.3d 1154, 1159, 47 USPQ2d 1829, 1833 (Fed. Cir. 1998), the disclosure of a species in the parent application did not suffice to provide written description support for the genus in the child application. Similarly, see *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989) (generic and sub-generic claims in the U.S. application were not entitled to the benefit of foreign priority where the foreign application

disclosed only two of the species encompassed by the broad generic claim and the sub-generic Markush claim that encompassed 21 compounds).

[5] The Examiner contends that *In re Fuetterer* is not on point because the adequacy of the inventors' disclosure was never questioned (e.g., see *In re Fuetterer*, 138 USPQ 217, 223, "'therefore, as the examiner alleges, many an 'inorganic salt' would not be operative for appellant's purpose,' this criticism bears only on the sufficiency of the invention description. But its adequacy under the first paragraph of section 112 has not been questioned."). Here, the "adequacy" of the inventors' disclosure is being questioned and, as a result, Applicants' arguments are moot. In addition, the Examiner notes that the requirements have not been met with regard to the Written description guidelines and that this point has been adequately addressed in section **[1]** above.

The Examiner also notes that it is well settled that claiming only a result (i.e., the ability to selectively inhibit Cox-2 and/or LTB_4 inhibitors/antagonists) fails to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result, far beyond those means actually discovered or contemplated by the inventor, so that others would have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217 ; Siegel v. Watson, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119. Here, the breadth of Applicants' claims would impede the progress of science and the useful arts because it extends far beyond those means actually discovered or contemplated by the inventors.

[6] The Examiner contends Applicants arguments are broad enough to encompass both "known" and "unknown" compounds (e.g., see section **[1]** above wherein "antisense-oligonucleotides" was provided as an example of an "unknown" inhibitor and/or antagonist). Thus, Applicants' arguments are not commensurate in scope to the claims.

[7] The Examiner contends that Applicants' arguments are not commensurate in scope to the claims because Applicants' claims are broad enough to encompass "nucleic acids" (e.g., see section **[1]** above wherein "antisense-oligonucleotides" was provided as an example of an "unknown" inhibitor and/or antagonist) and thus *Eli Lilly* is not readily distinguishable. In addition, Applicants claims are broad enough to encompass many other classes of "unknown" compounds (e.g., see 35 U.S.C. 112, second paragraph rejections, which are incorporated in their entirety herein by reference) and, as a result, "generic formulas" have not been provided for the full scope of the claimed invention (i.e., the recited passage proves that Applicants' are not in possession of the full scope of the claimed genus). It should also be noted that the Written Description Requirements have not been met and that these points have been adequately addressed in section **[1-3]** above. Finally, the Examiner notes that it means little to "invent" a composition comprising compounds A and B if one does not have possession of compounds A and B that are essential to make the composition. Without those compounds, the claimed invention is more theoretical than real; it is, as defendants argue, akin to "inventing" a cure for cancer by utilizing a composition that attacks and destroys cancer cells while leaving healthy cells alone. Without possession of the compounds that make up said composition, such a "cure" is illusory, and there is no meaningful possession of the composition.

[8] The Examiner finds Applicants' arguments persuasive with regard to claim 8 because both compounds are structurally defined. However, with regard to claims 2, 6, 7 and 9, the Examiner contends that the functional language is not adequate supported for the reasons of record.

[9] The Examiner respectfully contends that Applicants' interpretation of *Rochester* is too narrow and inconsistent with the cited passages. For example, Applicants quote Rochester as follows, "At best, it simply indicates that one should run tests on a wide spectrum of compounds in the hope that at least one of the will work" (e.g., see 12/17/03 Response, page 33, last paragraph). This quote clearly indicates that if the specification does not provide any guidance other than "trial and error" testing to determine whether a compound will or will not have a desired result than such a specification fails to meet the Written Description Guidelines. Here, the vast majority of Applicants' claimed compounds (i.e., all the compounds that are not structurally related to the 100 examples of Cox-2 inhibitors and 40 examples of LTB_4 antagonists) would fall within this category because the specification does not provide any other structural correlations and/or identifying features that would lead a person of skill in the art to the claimed compounds. For example, nothing in Applicants' specification would lead a person of skill in the art to an anti-sense DNA/RNA molecule. These anti-sense DNA/RNA molecules are not structurally related to any Cox-2/LTB_4 examples provided by Applicants and Applicants do not provide any other identifying features that would lead a person of skill in the art to this class of compounds or any species falling within this class. This interpretation is also consistent with cases like *In re Herschler* because more than one "core structure" is being claimed in the present case (i.e., a greater showing is required in a less predictable art).

[10] The Examiner has already acknowledged that there are many ways to adequately describe a claimed invention (e.g., see section **[1]**) and believes that Applicants arguments with regard to providing "relevant structural chemical formulas" and "detailed" definitions, etc. have been adequately addressed above (e.g., see sections **[1-3]**).

Accordingly, the written description rejection cited above is hereby maintained.

Claims Rejections - 35 U.S.C. 112, second paragraph

5. Claims 1-4, 6, 7, 9, 11, 15, 16, 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1-4, 6, 7, 9, 11, 15, 16, 17 and 18 are rejected because the compounds in these claims are not defined with any chemical or physical characteristic, but only by functional properties i.e., that they are either a "cyclooxgenase-2 selective inhibitor" or a "selective leukotriene B_4 receptor antagonist." A claim to a material defined solely in terms of what it can do, or a property thereof, does not particularly point out the claimed invention. A person of skill in the art cannot immediately envision all the possible chemical structures for a compound with this function. See *ex parte Pulvari* (POBA 1966) 157 USPQ 169. Here, the Examiner contends that no correlation between structure and function has been presented for either the Cox-2 inhibitor or the leukotriene B_4 receptor antagonist and, as a result, a person of skill in the art would not be able to "immediately envision all the possible chemical structures" for either the Cox-2 inhibitor

or the leukotriene B_4 receptor, which is further supported by the widely varying structures claimed by Applicants. Furthermore, Applicants have not set forth the conditions under which the "selective activity" is to be measured further compounding the problem. Thus, the metes and bounds of the claimed invention cannot be determined.

Response

6. Applicant's arguments directed to the above 35 U.S.C. 112, second paragraph rejections were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or newly amended arguments.

A. Applicants argue that they have provided a "comprehensive disclosure" in accordance with MPEP 2173.02, which renders the claims definite under 35 USC 112, second paragraph (e.g., see 12/17/03 Response, pages 36-37) and specifically refer to the 140 examples of Cox-2/LTB_4 inhibitors disclosed therein and the passages that define the binding assays and/or affinities that were used to characterize said inhibitors).

This is not found persuasive for the following reasons:

The Examiner contends that Applicants have not provided a "comprehensive" disclosure for the "selective" Cox-2/LTB_4 inhibitors/antagonists as purported. For example, Applicants' specification does not even define the term "selective" Cox-2 (or LTB_4) inhibitor/antagonist and, as a result, it is not clear what compounds should be

considered "selective" because "selective" is a "relative" term (e.g., see 35 USC 112, second paragraph rejection below (i.e., rejection B), which is incorporated in its entirety herein by reference). The passages cited by Applicants (e.g., see 12/17/03 Response, page 36) notably fail to draw the reader's attention toward the most important parts of the definitions, namely, the subject matter of what is being defined (e.g., see 12/17/03 Response, page 36, wherein the cited passages omit the first sentence of each definition). In both cases, Applicants define (referring to the full definition in the specification) only broad categories of Cox-2/LTB_4 inhibitors/antagonists that "embrace" selective inhibitors/antagonists as well as non-selective inhibitors/antagonists (e.g., see page 7, lines 28-29, "The term 'cyclooxygenase-2 inhibitor' embraces [i.e., comprise] compounds which selectively inhibit cyclooxygenase-2 ..."; see also page 8, lines 4-5, "The term 'leukotriene B_4 receptor antagonist' embraces [i.e., comprise] compounds which selectively antagonize a leukotriene B_4 receptor ..."). These definitions include both "selective" and "non-selective" inhibitors/antagonists because Applicants use "comprising" terminology that does not preclude the "non-selective" inhibitors/antagonists from falling within the scope of the definitions (e.g., see Webster's II New Riverside University Dictionary, page 427, wherein the dictionary defines "embrace" as "... **3.** To include, comprise, or contain"). That is Applicants are not defining what "selective" Cox-2/LTB_4 inhibitors/antagonists are but, rather, what Cox-2/LTB_4 inhibitors are in general (i.e., whether they are selective or non-selective). In addition, the selectivity ratios and/or IC_{50} values referred to by Applicants represent only "preferred" embodiments and, as a result, are not limitations that are "required" (e.g., see

page 12/17/03 Response, page 36, "Preferably, the compounds have a cycloxygenase-2 IC_{50} of less than about 0.5 μM ..."). Thus, the functional language is indefinite because nothing in Applicants' specification provides a definition, structural correlation and/or any other means of curing the defects for Applicants' claimed functional language (see 35 U.S.C. 112, second paragraph rejection above).

In addition, the Examiner notes that it is well settled that claiming only a result (i.e., the ability to selectively inhibit Cox-2 and/or LTB_4 inhibitors/antagonists) fails to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result, far beyond those means actually discovered or contemplated by the inventor, so that others would have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217 ; Siegel v. Watson, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119 . Thus a material defined, as here, solely in terms of what it can do (i.e., functional language with nothing more) does not particularly point out, as required by 35 U.S.C. 112, second paragraph, the disclosed invention.

Finally, the Examiner notes that Applicants specification is misleading (i.e., apparently filled with many mistakes) because it discloses compounds like "MK-866" as "preferred" LTB_4 antagonists (e.g., see specification, paragraph bridging pages 8-9, "Preferred leukotriene B_4 receptor antagonists include ... MK-886") (emphasis added), but then Applicants in their arguments explicitly disclaim MK-866 from being classified as a LTB_4 receptor antagonist, let alone a "preferred" antagonist (e.g., see 12/17/03

Response, page 41, first sentence, "Significantly, a selective leukotriene B4 antagonist is not the same thing as a 5-lipoxygenase inhibitor such as MK-866"). Thus, Applicants specification only serves to further confuse the definition of a "selective" Cox-2 and/or LTB_4 inhibitor/antagonist.

Accordingly, the 35 U.S.C. 112, second paragraph rejection cited above is hereby maintained.

Claim Rejections - 35 USC § 103

7. Claims 1-2 and 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ducharme et al. (US Pat. No. 5,474,995) (Filing Date is **January 10, 1994**; Date of Patent is **December 12, 1995**) (IDS Reference Number 60) and Rainsford, K. D. (Rainsford, K. D. "Leukotrienes in the pathogenesis of NSAID-induced gastric and intestinal mucosal damage" *Agents and Actions* **1993**, 39 (Spec. Conf. Issue), C24-C26).

For ***claims 1-2 and 6-9***, Ducharme et al. teach cycloxgenase-2 inhibitors and pharmaceutical compositions thereof with compounds of Formula I (e.g., see Ducharme et al. i.e., "1 of 2", Summary of Invention; see also Ducharme et al. "2 of 2", showing various compounds that fall within the scope of Formula I). For example, Ducharme et al. teach a Cox-2 inhibitory (see Ducharme et al., "2 of 2", page 3, RN 157671-80-2) with the same formula as that claimed by applicants in Formula I of claim 2 wherein R^2 is an methyl, A is a furan ring (i.e., furyl), R^1 is a phenyl substituted with a fluoro, and R^3 is a hydrido (Please note that other examples also exist as shown throughout Ducharme et al., "2 of 2"). Ducharme et al. also teaches that the above compounds of formula I "will be

useful as a partial or complete substitute for conventional NSAID's in preparations wherein they are presently co-administered with other agents or ingredients" (see Ducharme et al., "1 of 2", column 7, lines 65-67).

The prior art teachings of Ducharme et al. differ from the claimed invention as follows:

For **claim 1-2 and 6-9**, Ducharme et al. are deficient in that although it states that the Cox-2 inhibitors of formula I "will be useful as a partial or complete substitute for conventional NSAID's in preparations wherein they are presently co-administered with other agents or ingredients" (see Ducharme et al., "1 of 2", column 7, lines 65-67), Ducharme et al. does not explicitly state that NSAID's are presently co-administered with the leukotriene B_4 antagonists disclosed by applicants. Hence, Ducharme et al. are deficient in that it does not teach that the Cox-2 inhibitors of formula I "will be useful" as "substitutes" for NSAID's in preparations where NSAID's and leukotriene B_4 antagonists are co-administered, which would make the required "combination" of Cox-2 inhibitors and leukotriene B_4 antagonists.

However, Rainsford teaches the following limitations that are deficient in Ducharme et al.:

For ***claims 1-2 and 6-9***, Rainsford teaches that the leukotriene B_4 receptor antagonist, MK-886, can be beneficially co-administered with NSAIDs (see Rainsford, abstract) ("Gastric and intestinal mucosal lesions by NSAIDs were prevented by both prior (2-5 h) + 0.25 or 0 h oral dosing of the 5-lipoxygenase inhibitor, MK-886", which are identical to figure 2 and similar to figure 10 of the specification). Hence, the

combined teachings of Ducharme et al. and Rainsford would teach a "combination" of Cox-2 inhibitors of formula I (i.e., Cox-2 inhibitors are "substituted" for the NSAIDs) with leukotriene B_4 receptor antagonists like MK-886. Furthermore, it would have been obvious to use other "known" Cox-2 and Leukotriene B_4 antagonists as outlined in claims 4, 8 and 9 because they would have the same effect (i.e., they would also be Leukotriene B_4 antagonists or Cox-2 inhibitors and thus would have the same therapeutic value when used in combination).

It would have been obvious to one skilled in the art at the time the invention was made to "substitute" the compounds of formula I as taught by Ducharme et al. for the NSAIDs in the preparations containing both NSAIDs and leukotriene B_4 antagonists (i.e., MK-886) as taught by Rainsford because Ducharme explicitly states that "compounds of formula I, will be useful as a partial or complete substitute for conventional NSAID's in preparations wherein they are presently co-administered with other agents or ingredients" (see Ducharme et al., column 7, lines 65-67). Furthermore, one of ordinary skill in the art would have been motivated to use the Cox-2 inhibitors and Leukotriene B_4 inhibitors to further lower the gastric mucosal lesions that occur with NSAIDs, while still maintaining the therapeutic effects (see Ducharme et al., column 7, lines 50-65) ("By virtue of its high cycloxygenase-2 (Cox-2) activity and/or its selectivity for cyclooxygenase-2 over cyclooxygenase-1 (Cox-1) as defined above, compounds of formula I will prove useful as an alternative to conventional non-steroidal anti-inflammatory drugs (NSAID'S) particularly where such non-steroidal anti-inflammatory drugs may be contra-indicated such as in patients with peptic ulcers").

Response

8. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue that MK-866 is not a "selective" LTB_4 antagonist and thus the combined references do not render obvious the currently claimed invention (e.g., see 12/17/03 Response, pages 40-42).

This is not found persuasive for the following reasons:

The Examiner contends that Applicants have not provided a clear definition for a "selective LTB_4 antagonist" (e.g., see 35 U.S.C. 112, second paragraph rejections denoted A and B, which are incorporated in their entirety herein by reference) and, as a result, Applicants' arguments are moot. In addition, the Examiner notes that the specification explicitly states that MK-866 is a "preferred" LTB_4 antagonist (e.g., see paragraph bridging pages 8-9, especially page 9, line 1). Thus, Applicants' arguments are inconsistent with the teachings in their specification. In addition, the Examiner notes that there is no requirement in Applicants' current claims that the production of ***only*** leukotriene B_4 be inhibited as Applicants purport (e.g., see 12/17/03 Response page 41, last paragraph) and, as a result, Applicants' arguments are also not commensurate in scope with the claims.

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

New Rejections

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-4, 6, 7, 9, 11, 15, 16, 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

B. Claim 1-4, 6, 7, 9, 11, 15 and 16 recite the term "selective." The term "selective" is a relative term, which renders the claim indefinite and/or unclear. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See also MPEP § 2173.05(b). Applicants' specification does not provide a means for ascertaining the requisite degree because Applicants only disclose "preferable" examples without explicitly stating that a degree for selectivity is "required" (**Please note**: the definitions for Cox-2/LTB_4 inhibitors/antagonists listed on pages 7-8 do not provide a definition for "selective" inhibitors/antagonists and the assays and binding affinities cited therein represent only "preferable" examples that do not limit the definition of a "selective" inhibitor e.g., see 35 USC 112, second paragraph rejection above (i.e., rejection A), which is incorporated in its entirety herein by reference).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-2, 9 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buchmann et al. (WO 94/04522) (Publication Date is **March 3,1994**) (Please note: this reference has the same translation as that of U.S. Patent No. 5,559,134 cited below) (of record) and Futaki et al. (Futaki, N.; Takahashi, s.; Yokoyama, M.; Arai, I.; Higuchi, S.; Otomo, S. "NS-398, a new anti-inflammatory agent, selectively inhibits prostaglandin G/H synthase/cycloxygenase (COX-2) activity in vitro" Prostaglandins **1994**, 47, 55-59).

For ***claims 1-2, 9 and 17-18***, Buchmann et al. disclose "new leukotriene-B_4 derivatives ... used in combination ... with cyclooxygenase inhibitors" (see Buchmann et al., page 11, lines 58-65; see also claims 1, 2 and 10), which reads on claim 1. Although the compounds in the Buchmann et al. reference do not explicitly state that the LTB_4 antagonists are "selective" antagonists they share a reasonably close correlation to the structures that are taught in Applicants' disclosure (e.g., they fall within the class of "aryl ethers" as disclosed in Applicants' specification at, page 3, first full paragraph; see also specific examples of "aryl ethers" listed in claims like Lilly LY-293111). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office ***does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference***. See *In re Best,* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

The prior art teachings of Buchmann et al. differ from the claimed invention as follows:

For ***claims 1-2, 9, 17-18***, Buchmann et al. are deficient in that they do not specifically teach the use of a "selective" Cox-2 inhibitor. Buchmann et al. only teach the use of Cox-2 inhibitors, but they do not provide a specific example (see Buchmann et al., Buchmann et al., page 11, lines 58-65; see also claims 1, 2 and 10).

However, Futaki et al. teach the following limitations that are deficient in Buchmann et al.:

For ***claims 1-2, 9, 17-18***, Futaki et al. (see entire document) teach the use of NS-398, which is a selective Cox-2 inhibitor with an IC_{50} value being 3.8×10^{-6} M versus its Cox-1 inhibition at 10^{-4} M. Furthermore, Futaki et al. teach (see Futaki et al., abstract; Please note that Cox-2/Cox-1 IC_{50} ratio is "at least 100").

It would have been obvious to one skilled in the art at the time the invention was made to use the Cox-2 inhibitors as taught by Futaki et al. with the LTB_4 antagonists as taught by Buchmann et al. because Buchmann et al. explicitly states that the LTB_4 antagonists can be combined with the Cox-2 inhibitors (e.g., Buchmann et al., Buchmann et al., page 11, lines 58-65; see also claims 1, 2 and 10). A person of skill in the art would have been motivated to use the "selective" Cox-2 inhibitors because Futaki et al. state that NS-398 "produced much smaller gastrointestinal lesions" than other "non-selective" Cox-2 inhibitors like indomethacin which would result in "less gastrointestinal toxicity" (e.g., see page 55 abstract; see also page 56, paragraphs 1-2). Furthermore, a person of skill in the art would have reasonably expected to be successful because Futaki et al. state that NS-398 is "almost as potent as indomethacin [i.e., a non-selective Cox-2 inhibitor]" and thus would be expected to act in a similar fashion (e.g., see Futaki et al., abstract).

12. Claims 1-2, 9 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buchmann et al. (US Pat. No. 5,559,134) (Filing Date is **March 23, 1995**; Date of Patent is **September 24, 1996**) (of record) and Futaki et al. (Futaki, N.; Takahashi, s.; Yokoyama, M.; Arai, I.; Higuchi, S.; Otomo, S. "NS-398, a new anti-inflammatory agent, selectively inhibits

prostaglandin G/H synthase/cycloxygenase (COX-2) activity in vitro" Prostaglandins **1994**, 47, 55-59).

For ***claims 1-2, 9 and 17-18***, Buchmann et al. disclose "new leukotriene-B_4 derivatives ... used in combination ... with cyclooxygenase inhibitors" (see Buchmann et al., page column 7, lines 58-65; see also claims 1, 2 and 10), which reads on claim 1. Although the compounds in the Buchmann et al. reference do not explicitly state that the LTB_4 antagonists are "selective" antagonists they share a reasonably close correlation to the structures that are taught in Applicants' disclosure (e.g., they fall within the class of "aryl ethers" as disclosed in Applicants' specification at, page 3, first full paragraph; see also specific examples of "aryl ethers" listed in claims like Lilly LY-293111). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office ***does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference***. See *In re Best,* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

The prior art teachings of Buchmann et al. differ from the claimed invention as follows:

For ***claims 1-2, 9, 17-18***, Buchmann et al. are deficient in that they do not specifically teach the use of a "selective" Cox-2 inhibitor. Buchmann et al. only teach

the use of Cox-2 inhibitors, but they do not provide a specific example (see Buchmann et al., Buchmann et al., page column 7, lines 58-65; see also claims 1, 2 and 10).

However, Futaki et al. teach the following limitations that are deficient in Buchmann et al.:

For ***claims 1-2, 9, 17-18***, Futaki et al. (see entire document) teach the use of NS-398, which is a selective Cox-2 inhibitor with an IC_{50} value being 3.8×10^{-6} M versus its Cox-1 inhibition at 10^{-4} M. Furthermore, Futaki et al. teach (see Futaki et al., abstract; Please note that Cox-2/Cox-1 IC_{50} ratio is "at least 100").

It would have been obvious to one skilled in the art at the time the invention was made to use the Cox-2 inhibitors as taught by Futaki et al. with the LTB_4 antagonists as taught by Buchmann et al. because Buchmann et al. explicitly states that the LTB_4 antagonists can be combined with the Cox-2 inhibitors (e.g., Buchmann et al., Buchmann et al., page column 7, lines 58-65; see also claims 1, 2 and 10). A person of skill in the art would have been motivated to use the "selective" Cox-2 inhibitors because Futaki et al. state that NS-398 "produced much smaller gastrointestinal lesions" than other "non-selective" Cox-2 inhibitors like indomethacin which would result in "less gastrointestinal toxicity" (e.g., see page 55 abstract; see also page 56, paragraphs 1-2). Furthermore, a person of skill in the art would have reasonably expected to be successful because Futaki et al. state that NS-398 is "almost as potent as indomethacin [i.e., a non-selective Cox-2 inhibitor]" and thus would be expected to act in a similar fashion (e.g., see Futaki et al., abstract).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-4, 6, 7, 9, 11, 15, 16, 17 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,172,096 (referred to herein as '096) (especially claims 1 and 6). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the referenced patent are essentially drawn to same type of "combinations" of therapeutic compounds as the present application. For example, the '096 patent claims a method for combining a therapeutically-effective amount of a leukotriene B_4 (LTB_4) receptor antagonist and a cycloxygenase-2 inhibitor (Cox-2) which would render obvious the composition produced by said method i.e., a composition of a Cox-2 and LTB_4 inhibitors/antagonists (see '096 patent, claim 1). The '096 patent differs from the presently claimed invention by not reciting the use of "selective" Cox-2/LTB_4 inhibitors/antagonists (e.g., compare claim 1 of '096 to claim 1 of the present application). However, it would have been obvious to use "selective" Cox-2/LTB_4 inhibitors in view of the '096 patent claims because the '096 patent in many cases claims the same "selective" Cox-2/LTB_4 inhibitors/antagonists as does the present application (e.g.,

compare claim 1 of '096 to claim 2 of the present application wherein the same "formula I" compounds are claimed as LTB_4 antagonists; compare also claim 6 of '096 to claim 8 of the present application wherein 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl] benzenesulfonamide is claimed in both Applications as a "selective" Cox-2 inhibitor). In addition, Applicants provide the same definition in the '096 patent for Cox-2/LTB_4 antagonists/inhibitors as does the present application, which includes, for example, many "selective" inhibitors and/or antagonists as "preferred" embodiments (e.g., compare '096 definition at column 6, lines 39-54 to definition in present application at bottom of page 7 and top of page 8; compare also columns 7-8 of '096 to pages 8-10 of the present application wherein TMK-688, Bay-X-1005, ONO-4057, LY-293111, ETC-615, Meloxicam, Flosulide, NS-398 are disclosed in both references). Accordingly it is deemed that the inventions claimed herein and that of the patent are obvious variants of each other. A person of skill in the art would have been motivated to use the "selective" inhibitors because the '096 patent claims the same "selective" inhibitors as "preferred" embodiments and further defines the Cox-2/LTB4 inhibitors/antagonists to encompass the same "selective" compounds.

14. Claims 1-4, 6, 7, 9, 11, 15, 16, 17 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,617,345 (referred to herein as '345) (especially claims 1-2). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the referenced patent are essentially drawn to same type of "combinations" of therapeutic compounds as the present application i.e., a composition of a Cox-2 and LTB_4

inhibitors/antagonists (e.g., see '345 patent, claim 1). The '345 patent differs from the presently claimed invention by not reciting the use of "selective" Cox-2/LTB_4 inhibitors/antagonists (e.g., compare claim 1 of '345 to amended claim 1 of present application). However, it would have been obvious to use "selective" Cox-2/LTB_4 inhibitors in view of the '345 patent claims because the '345 patent in many cases claims the same "selective" Cox-2/LTB_4 inhibitors/antagonists as does the present application (e.g., compare claim 1 of '345 to claim 2 of the present application wherein the same "formula I" compounds are claimed as LTB_4 antagonists; compare also claim 2 of '345 application to claim 3 of the present application wherein Bay-x-1005, ONO-4057, ETH-615, etc are disclosed as LTB_4 antagonists; compare also claim 1 of '345 to claim 2 of the present application wherein meloxicam, fluosilide, Taisho NS-398, etc. are disclosed as Cox-2 inhibitors in both references). In addition, Applicants provide the same definition in the '345 patent for Cox-2/LTB_4 antagonists/inhibitors as does the present application, which includes, for example, many "selective" inhibitors and/or antagonists as "preferred" embodiments (e.g., compare '345 definition at column 6, lines 39-54 to definition in present application at bottom of page 7 and top of page 8). Accordingly it is deemed that the inventions claimed herein and that of the patent are obvious variants of each other. A person of skill in the art would have been motivated to use the "selective" inhibitors disclosed in the '345 patent because these "selective" inhibitors are disclosed in the claims, which represent preferred embodiments.

15. Claims 1-4, 6, 7, 9, 11, 15, 16, 17 and 18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. US 2004/0106668 A1 (referred to herein as '668) (especially claims 1-2).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the referenced patent are essentially drawn to same type of "combinations" of therapeutic compounds as the present application i.e., they "comprise" a composition of a Cox-2 and LTB_4 inhibitor/antagonist (e.g., compare '668 patent, claim 1 to claim 1 of the present application) (Please note that the fact that the 668 patent also claims a "immunosuppressive drug" does not detract from this rejection because Applicants use "comprising" terminology in the present Application that would not preclude the addition of such a drug). The '668 patent differs from the presently claimed invention by not reciting the use of "selective" Cox-2/LTB_4 inhibitors/antagonists (e.g., compare claim 1 of '668 to amended claim 1 of present application). However, it would have been obvious to use "selective" Cox-2/LTB_4 inhibitors in view of the '668 patent claims because the '668 patent in many cases claims the same "selective" Cox-2/LTB_4 inhibitors/antagonists as does the present application (e.g., compare claim 2 of '668 to claim 2 of the present application wherein the same "formula I" compounds are claimed as LTB_4 antagonists; compare also claim 3 of '668 application to claim 3 of the present application wherein Bay-x-1005, ONO-4057, ETH-615, etc are disclosed as LTB_4 antagonists; compare also claim 2 of '668 to claim 2 of the present application wherein meloxicam, fluosilide, Taisho NS-398, etc. are disclosed as Cox-2 inhibitors in both references). In addition, Applicants provide the same definition in the '668 patent for Cox-2/LTB_4 antagonists/inhibitors as does the present application, which includes, for example, many "selective" inhibitors and/or antagonists as "preferred" embodiments (e.g., compare '668 definition at paragraphs 25-26 to definition in present application at bottom of page 7 and top of page 8). Accordingly it is deemed that the inventions claimed herein and that of the patent are obvious variants of each other. A person of

skill in the art would have been motivated to use the "selective" inhibitors disclosed in the '668 patent because these "selective" inhibitors are disclosed in the claims, which represent preferred embodiments.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
July 17, 2004

BENNETT CELSA
PRIMARY EXAMINER